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| 10/560,455      | 12/14/2005  | Silvia Gluck         | 13111-00027-US      | 3072             |

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| EXAMINER |
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MARX, IRENE

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| ART UNIT | PAPER NUMBER |
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1651

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08/13/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/560,455

**Applicant(s)**

GLUCK ET AL.

**Examiner**

Irene Marx

**Art Unit**

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 5, 6 and 18-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5-6 and 18-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/5508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

#### DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/9/09 has been entered.

Claims 1, 5-6 and 18-21 are being considered on the merits.

#### *Claim Rejections - 35 USC § 112*

Claims 1, 5-6 and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ strains of *Lactobacillus* or *Lactococcus* to obtain a specific product. The written description of that strain and the method of isolating is insufficiently reproducible. Therefore, a deposit for patent purposes is required. The specification discloses at page 39 that specific strains were deposited at DSMZ under Budapest Treaty conditions on 11 July 2003.

For compliance with the rule, it must be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g. see 961 OG 21, 1977) and that **all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.** MPEP 2403.

It is unclear whether such a statement is of record in the present record.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-6 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague, indefinite and confusing in that the preamble recites the microbiological isomerization of a large number of compounds while the body of the claim is directed to an isomerization wherein *Lactobacillus* or *Lactococcus* are "capable" of racemizing at least one compound selected from only five compounds. The correlation between the recited capabilities of the microorganisms and the broad class of compounds intended to be bioconverted cannot be readily ascertained.

Claim 6 is vague, indefinite and confusing in the use of parenthetical DSM accession numbers. It is uncertain which of the two numbers is the actual accession number accorded by the DSM. Clarification is required. It is recommended that no parenthetical recitation be provided, since it is unclear whether the parenthetical material is or is not intended to be part of the claim.

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-6 and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stetter *et al.*, taken with DSMZ Catalogue, Mori *et al.* and Seuffer-Wasserthal *et al.* (U.S. Patent No. 5,534,436).

The claims are directed to a process of isomerization of an  $\alpha$ -hydroxycarboxylic acid with an enzyme in a reaction medium, wherein the enzyme is contained in an extract or present in intact cells of a *Lactobacillus* or *Lactococcus* and optionally isolating the mixture obtained and chemical or enzymatically treating it further.

Stetter *et al.* discloses a process of isomerization an  $\alpha$ -hydroxycarboxylic acid with *Lactobacillus* strains *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. delbrueckii*

ATCC 9649 which is identical to DSM 20074 (DSM 15754) and *L. sakei* ATCC 15521, which is identical to DSM 20017 (DSM 15753) in the process (See, e.g., page 225-226 and Figure, page 237), as adequately demonstrated by DSMZ Catalogue, see, e.g., item 906, which is the Stetter *et al.* reference and applicant's proffer. It is clear that at least these three *Lactobacillus* strains contain the enzymatic activity required for the claimed process and are capable thereof..

The reference differs from the claimed invention in the substrates submitted to the isomerization reaction. However, one of ordinary skill in the art would have recognized at the time the claimed invention was made that the substrate specificity of the enzyme extracts or microbial cells provided by Stetter *et al.* is not limited to the disclosed substrate and would have been motivated to test further substrates with a reasonable expectation of success by using microbial enzymes from *Lactobacillus* including the enzymes produced by or present in the extracts or cells of the strains recited, including *L. paracasei* subsp. *paracasei* DSM 20207 (DSM 15755), *L. sakei* ATCC 15521, DSM 20017 (DSM 15753) and *L. delbrueckii* ATCC 9649, DSM 20074 (DSM 15754) which are clearly inherently "capable" of isomerizing at least one compound from the list in claim 1, since they are strains indicated as particularly suitable in the process in the as filed specification. In addition, Mori *et al.* suggest further substrates in their teachings that products such as D-mandelic acid are useful as raw materials or intermediates in the preparation of pharmaceuticals such as antibiotics and ephedrin. See, e.g., page 2, lines 2-4.

The reference differs from the invention as claimed in that further enzymatic or chemical modifications are not recited. However, Mori *et al.* adequately show that it was well known in the art at the time the claimed invention was made to modify compounds obtained in isomerization or resolution reactions by converting a racemic compound into an optically active isomer. See, e.g., Examples. In addition, Seuffer-Wasserthal *et al.* disclose the chemical or enzymatic enantioselective subsequent reaction that comprises esterification. See, e.g., col. 2, bridging paragraph between col. 2 and 3.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Stetter *et al.* by using a variety of *Lactobacillus* strains and substrates such as mandelic acid, as suggested by Mori *et al.* and submitting the resultant product to further reactions such as esterification as suggested by the teachings of Mori *et al.* and Seuffer-Wasserthal *et al.* for the expected benefit of obtaining

pharmaceutically valuable optically active compounds that are important *per se* or which are useful intermediates to produce further optically active pharmaceuticals.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

### ***Response to Arguments***

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Applicant(s) argue(s) that there is no suggestion to combine references because Mori *et al.* teaches a two step reaction and does not disclose that *Lactobacillus* or *Lactococcus* are suitable for the first step of converting mandelic acid into benzoyformic acid. However, motivation can come not only from direct teaching of the prior art, but also the nature of the problem to be solved and/or the knowledge of persons of ordinary skill in the art, Ruiz v. A.B. Chance Co. 357 F.3d 1270, 69 USPQ2d 1686 (2004). In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ." Pp. 11–14. KSR INTERNATIONAL CO. v. TELEFLEX INC. ET AL. (2007). The cited references are in the same field of endeavour and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select components available in the prior art, *In re Winslow*, 151 USPQ 48 (CCPA, 1966). Further, the examiner recognizes that references cannot be arbitrarily combined that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references, *In re Nomiya*, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. One test for combining references is what the combination of disclosures taken as a whole would suggest to one versed in the art, rather than by their specific disclosures, *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In this case, Stetter *et al.*, Mori *et al.* and Seufer-Wasserthal *et al.* are all directed to the production of optically active compounds structurally related to lactate and which are useful for the production of pharmaceuticals. Mori *et al.*, for example, suggests that D-mandelic acid is a desirable product. Moreover, the secondary references are relied upon for their disclosure of knowledge in the art of the modification of compounds obtained in isomerization reaction or resolution reactions by converting a racemic compound into an optically active isomer and the disclosure of chemical or enzymatic enantioselective subsequent reaction that comprise esterification.

Even though Stetter does not disclose a bioconversion specific of the range of substrates of the present process by using extracts or cells of *Lactobacillus* or *Lactococcus*, it is submitted that the three disclosed strains of *Lactobacillus* are clearly "capable" of the bioconversion of further substrates as listed, even if this capacity is not explicitly disclosed in the reference. In addition, it is of interest to note that there is not a single *Lactococcus* strain is identified and shown in the present record to have the required bioconversion capability. Moreover, it is not apparent from the as-filed specification that any and all *Lactobacillus* or any and all *Lactococcus* strains or even all strains within the broad species recited in claim 5 have the touted capabilities.

The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ 399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data is not commensurate in scope with the degree of protection sought by the claim.

Therefore the rejection is deemed proper and it is adhered to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Art Unit: 1651

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Irene Marx/  
Primary Examiner  
Art Unit 1651



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